



Testimony of V. Srini Srinivasan, Ph.D Vice President, Verification Program The United States Pharmacopeial Convention, Inc.

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Mr. Chairman, Representative Waxman, and Members of the Committee, I thank you for the opportunity to tell you how the United States Pharmacopeia (USP) helps consumers select supplements they can trust. Briefly, USP tests dietary supplements and awards the distinctive USP Verified mark to products that pass our rigorous tests for quality, purity, and potency. That USP Verified mark, which is pictured in the appendix, appears on more than 200 vitamin, mineral, amino acid, and botanical products in stores across America today. Like the familiar UL mark from Underwriters Laboratory or the ADA Seal from the American Dental Association, the USP Verified mark assures consumers that a respected independent body has examined the product against pre-defined standards and has found that it passes those standards.

To determine whether a dietary supplement is entitled to display the USP Verified mark, USP's Verification Program for Dietary Supplements (the Verification Program) subjects manufacturers to a thorough and rigorous manufacturing facility audit and scientific review of their manufacturing and quality control processes. Their finished dietary supplement products are tested for conformity with the product's labeling.

Before describing USP's Verification Program and its benefits in detail, I will provide you with background information about USP, its standard-setting activities, and the recognition of USP standards under federal law. I also should inform you that I am appearing today on behalf of USP. My written disclosure pursuant to the "Truth in Testimony" rule is attached.

I. USP as a Standards-Setting Organization

USP, a not-for-profit, non-governmental organization, has been developing standards for medicinal products since 1820. Today, our standards apply to drugs, dietary supplements, biological products, and medical devices. As a core element of USP's mission to promote the public health, USP publishes these standards in the *United States Pharmacopeia* and *National Formulary*, published together as the *USP-NF*.

12601 Twinbrook Parkway Rockville, MD 20852



USP's public standards, which define the analytical procedures that are necessary to identify and control the quality of compendial products, lead to improved consistency of products in the marketplace. This assurance of consistent quality allows healthcare providers and consumers to have increased confidence in their healthcare decisions. USP's public standards also allow manufacturers to use the best, most relevant, and science-based analytical procedures. *USP-NF* is updated continuously to ensure that the standards evolve with advances in science.

USP's standards are developed by experts in the field sitting on all-volunteer USP Expert Committees. Before becoming final, standards are available for public review and comment in the USP publication *Pharmacopeial Forum*. Ultimately, a USP Expert Committee determines whether a monograph will appear in the *USP-NF*. The combination of a body of experts and a public review process is designed to ensure the development of scientifically sound standards through an open, transparent and participatory process.

A. Standards for Dietary Supplements

Dietary supplement standards in the *USP-NF* usually are designed to ensure consistency of product, to eliminate foreign ingredients, and to provide reasonable certainty that the consumer is getting what he or she paid for. USP began acting on the public health need for standards for vitamins, minerals, and amino acid products in the late 1980s. USP's standards-setting for botanical products began after the passage of the Dietary Supplement Health and Education Act of 1994 (DSHEA). USP considers this activity a return to the organization's roots, as early volumes of the *USP* set standards for botanical products such as valerian, ginger, and chamomile.

Dietary supplement standards in the *USP-NF* appear either as an ingredient or product monograph or as a General Chapter.

1. Ingredient and Product Monographs

Ingredient monographs generally specify analytical methods that manufacturers must use for identification (to ensure that the product is what it says it is) and assay (to ensure that the product behaves chemically as it should). The analytical method set forth in the monograph may be adopted by manufacturers and regulatory bodies alike to ensure product quality.

The current *USP-NF* includes 66 monographs for botanical products such as echinacea, ginkgo biloba, garlic, and saw palmetto. It also includes 123 monographs for individual non-botanical dietary supplement ingredients (*e.g.*, vitamins and minerals) as well as class monographs for non-botanical dietary supplement products containing one or more ingredients. Class monographs provide general standards for over 850 vitamin and mineral products in the marketplace. They have been widely adopted by the dietary supplement industry and assure the quality of many dietary supplement products in the marketplace.



2. General Chapters

A procedure that is required by many individual product or ingredient monographs may be described in a stand-alone General Chapter. The individual monographs then may incorporate the General Chapter by reference. A number of *USP-NF* General Chapters apply to dietary supplements.

General Chapter <2750> Manufacturing Practices for Dietary Supplements, for instance, sets forth broad-based good manufacturing practices (GMPs). GMP compliance is critical to producing a high-quality product. The GMPs defined in the *USP*, which are based on drug manufacturing GMPs, are the most credible and stringent third-party GMP standards in the U.S.¹ Compliance with GMPs helps to prevent such problems as contamination, batch to batch product inconsistency, unsanitary manufacturing facilities, and errors in product labeling. GMPs also define requirements for documentation of manufacturing processes that can help manufacturers to track, identify, and solve manufacturing problems when they occur.

B. Legal Effect

The *USP* and *NF* are recognized as "official compendia" under the Federal Food, Drug, and Cosmetic Act. *USP-NF* standards are enforceable by FDA, and articles that fail to meet applicable standards are considered to be adulterated or misbranded under the law. USP itself does not enforce its standards.

Under DSHEA, in contrast, dietary supplements are required to meet *USP-NF* standards only if the product purports to meet those standards, *e.g.*, by including the designation "USP" in the ingredient name. A product may be misbranded under DSHEA if it claims to meet USP standards but in fact does not. Thus, while DSHEA also recognizes the *USP* and *NF* as official compendia, compliance with *USP-NF* standards, including GMPs, is entirely voluntary for dietary supplement manufacturers. And as is the case with drugs, USP's standards for dietary supplements are enforceable by FDA, not USP.

II. Verification Program for Dietary Supplements

After DSHEA became law, the number of dietary supplements available in the U.S. increased dramatically. Health care providers and pharmacists as well as consumers found it increasingly difficult to distinguish poor quality dietary supplements from those of higher quality. The need grew for clarity in the dietary supplement marketplace, but DSHEA does not provide any method for providing such clarity.

In response to the rising public health need, USP created a new program, separate from its standards-setting activities, to fill this gap in information: verification of the quality of dietary supplements through its voluntary Verification Program for Dietary Supplements. The Verification Program's uniqueness and value lie in USP's credibility and experience and in the rigorous testing program.

The GMPs defined in *General Chapter* <2750> in fact are more stringent than the dietary supplement GMPs proposed by FDA in 2003.

Under the Verification Program, USP evaluates and verifies supplements according to stringent standards for product purity, accuracy of ingredient labeling, and proper manufacturing practices. Products that meet the program's rigorous requirements are awarded the right to use the USP Verified mark.

The USP Verified mark helps assure consumers, health care professionals, and supplement retailers that the product:

- Has labeling that is accurate;
- Contains the ingredients stated on the label in the designated amount or strength;
- Contains ingredients that will release and dissolve so that the body may absorb them;
- Meets requirements for limits on potential contaminants; and
- Has been manufactured properly by complying with USP and proposed FDA standards for GMPs.

A. Evaluation of Products in the Verification Program

USP evaluates dietary supplements submitted to the Verification Program through (1) extensive laboratory testing; (2) comprehensive review of quality control and manufacturing documentation; and (3) evaluation of manufacturer compliance with USP and proposed FDA standards for GMP.

First, the supplements are tested against USP established standards for purity and for ingredient content and performance characteristics, *e.g.*, dissolution and disintegration. This testing is performed by USP's laboratories and other third-party laboratories with demonstrated expertise in evaluating the complex composition of vitamin, mineral, and botanical compounds.

Second, the manufacturer's documentation of its quality control procedures is reviewed. This review examines the product's compliance with applicable specifications for dietary ingredients, excipients, packaging and labeling materials, and the finished product. The review also examines the testing method(s) and reference materials used by the manufacturer, to ensure that they are appropriate and acceptable; the product's stability data, to ensure that the product will retain its quality throughout its marketed shelf life period; and the manufacturing documentation, to verify that the master formula, manufacturing process directions, packaging instructions, product labeling, and indication of quality assurance final release approval are acceptable.

Third, the manufacturing facilities are inspected for compliance with USP and proposed FDA standards for GMPs. The GMP review is detailed, but GMP compliance generally assures that the manufacturing is subject to careful oversight, preventing intentional or unintentional contamination of the products with unwanted additives.

If a product meets the Verification Program criteria, the manufacturer is entitled to use the USP Verified mark on the product's labeling. Thereafter, USP periodically will test off-theshelf lots of the product at random to ensure that they continue to meet the program's strict



standards. The manufacturing sites will be audited for GMP compliance on a three-year basis, with manufacturers required to conduct annual self-audits during the intervening years and report the results to USP for review.

B. Verification Program Experience and Supplement Issues Resolved

USP's Verification Program has had a clear and positive impact on the dietary supplement marketplace. We have verified more than 200 different products. Since the first USP Verified product reached store shelves in 2003, about 100 million bottles of dietary supplements bearing the USP Verified mark have become available in pharmacies and grocery stores nationwide. Our program has been applauded in the press, as the quotes in Appendix B illustrate. And consumer awareness continues to grow: The Healthbeat Interactive Survey conducted by the Natural Marketing Institute in September 2005 found that 25 million consumers recognize the mark.

The Verification Program provides a very real benefit for consumers. Consumers who purchase a dietary supplement product bearing the USP Verified mark can be assured that the product:

- Does not contain dietary ingredients other than those stated on the label;
- Does not contain mislabeled or potentially harmful amounts of supplement ingredients;
- Does not contain dangerous levels of contaminants; and
- Was manufactured using sanitary and well-controlled procedures.

Moreover, dietary supplement products will not be considered for the Verification Program if they contain ingredients with safety concerns, even though they may be legally marketed under DSHEA. Products that USP has refused to verify include gingko containing vinpocetine, ephedra, kava kava, comfry, and chaparral.

The Verification Program also has had a significant impact on the quality systems and manufacturing practices of participating companies. In order to meet the Verification Program standards, participating manufacturers have undertaken the following, among other actions:

- Additional testing for undesirable contaminants;
- Reformulation of products that fail to dissolve;
- Reformulation to ensure that the formulation provides 100% of label claim throughout the product's shelf life;
- Characterization and quantification of botanical marker compounds;
- Implementation of stability study protocols to establish appropriate expiration dating; and
- Labeling changes to ensure an accurate list and appropriate quantitative claims for the ingredients.

These measures have further improved the quality of dietary supplements in the marketplace, and have resulted in consumers receiving more accurate information about their supplements.



III. Conclusion

Since 1820, USP staff and volunteers have dedicated themselves to protecting and promoting public health. USP's Verification Program fills a void in the federal regulation of dietary supplements created by DSHEA and helps consumers make educated and confident dietary supplement choices in the marketplace. USP will continue to encourage dietary supplement manufacturers to take steps to assure that their products are high quality and consistent with their labeling. In the interest of public health, we also encourage manufacturers of all types of dietary supplements to submit their products to the USP Verification Program for stringent and scientifically sound third-party verification.



Appendix A: "USP Verified" Mark





Appendix B

- ∨ Wall Street Journal calls USP's "the most rigorous of the seals programs." (7/10/02)
- ∨ Los Angeles Times states that "the most extensive independent testing is being offered by U.S. Pharmacopeia." (2/18/02)
- ∨ New York Times says that "United States Pharmacopeia is the best known of the three certifiers, setting standards recognized by the Food and Drug Administration for 180 years." (1/2/02)
- ∨ San Diego Union Tribune says that "USP is the gold standard in dietary supplement verification." (7/15/02)
- ∨ *Prevention Magazine* says that the USP program is "a huge step in the right direction." (November 2002)
- ∨ Pharmacy Times states "Given the criteria established by USP for evaluating a product's worthiness to be awarded the DSVP symbol, pharmacists and patients can now to some extent be reassured as to the integrity of many dietary supplements. Notably, any product bearing the DSVP symbol meets both USP standards for inclusion in the National Formulary and established safety standards." (April, 2003)



Truth in Testimony Disclosure

Government grants, subgrants, and contracts awarded to V. Srini Srinavasan personally in the current or past 2 fiscal years: None

Non-governmental entity being represented: The United States Pharmacopeial Convention, Inc.

Government grants, subgrants, and contracts awarded to the represented entity in the current or past 2 fiscal years:

FY04

| Agency | Program | Amount |
|--|---|-------------|
| United States Agency for International | Drug Quality and Information Project | \$1,881,080 |
| Development | | |
| National Institute of Child Health and | Drugs without pediatric labeling review | \$54,990 |
| Human Development | | |

FY05

| Agency | Program | Amount |
|--|--------------------------------------|-------------|
| United States Agency for International | Drug Quality and Information Project | \$2,280,429 |
| Development | | |
| Centers for Medicare and Medicaid | Development of Drug Classes and | \$1,150,442 |
| Services | Categories in Part D | |

FY06 to date (Current)

| Agency | Program | Amount |
|--|--------------------------------------|-------------|
| United States Agency for International | Drug Quality and Information Project | \$1,826,211 |
| Development | | |
| Centers for Medicare and Medicaid | Medicare Part D (subcontract) | \$44,121 |
| Services | | |